

We claim:

1. A purified polypeptide that binds to neoplastic cells, wherein said polypeptide has an amino acid sequence substantially identical to the sequence of SEQ ID NO 1 and/or SEQ ID NO 3, and wherein said polypeptide specifically binds to BXPC-3 (ATCC Accession No. CRL-1687), 23132/87 (DSMZ Accession No. ACC 201), COLO-206F (DSMZ Accession No. ACC 21), COLO-699 (DSMZ Accession No. ACC 196), and LOU-NH91 (DSMZ Accession No. ACC 393) cells and not to non-neoplastic cells.
2. A purified polypeptide that binds to neoplastic cells, wherein said polypeptide has an amino acid sequence substantially identical to the sequence of SEQ ID NO 1 and/or SEQ ID NO 3, and wherein said polypeptide specifically binds to BXPC-3 (ATCC Accession No. CRL-1687), 23132/87 (DSMZ Accession No. ACC 201), COLO-206F (DSMZ Accession No. ACC 21), COLO-699 (DSMZ Accession No. ACC 196) and LOU-NH91 (DSMZ Accession No. ACC 393) cells and not to non-neoplastic cells, and wherein said neoplastic cell is a adenocarcinoma of the lung, squamous cell lung carcinoma, intestinal type gastric carcinoma, diffuse type gastric carcinoma, adenocarcinoma of the colon, adenocarcinoma of the prostate, squamous cell carcinoma of the esophagus, adenocarcinoma of the esophagus, adenocarcinoma of the esophagus lobular carcinoma of the breast, ductal carcinoma of the breast, adenocarcinoma of the pancreas, adenocarcinoma of the ovary, and adenocarcinoma of the uterus cell.

- 5 3. A purified polypeptide that binds to neoplastic cells, wherein said polypeptide has an amino acid sequence substantially identical to the sequence of SEQ ID NO 1 and/or SEQ ID NO 3, and wherein said polypeptide specifically binds to a adenocarcinoma of the lung, squamous cell lung carcinoma, intestinal type gastric carcinoma, diffuse type gastric carcinoma, adenocarcinoma of the colon, adenocarcinoma of the prostate, squamous cell carcinoma of the esophagus, adenocarcinoma of the esophagus, lobular carcinoma of the breast, ductal carcinoma of the breast, adenocarcinoma of the pancreas, adenocarcinoma of the ovary, and adenocarcinoma of the uterus cell and not to a non-neoplastic cell.
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- 15 4. The purified polypeptide of claim 1, 2 or 3, wherein said polypeptide inhibits cell proliferation when bound to a neoplastic cell, but does not inhibit cell proliferation of a non-neoplastic cell.
- 20 5. The purified polypeptide of claim 1, 2 or 3, wherein said polypeptide
- binds to low density lipoproteins (LDL) and/or oxidised low density lipoproteins (oxLDL), and/or
  - binds to very low density lipoproteins (VLDL), and
  - induces the intracellular accumulation of lipids when bound to a neoplastic cell, but does not induce the intracellular accumulation of lipids in a non-neoplastic cell.
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6. The purified polypeptide of claim 1, 2 or 3, wherein said polypeptide induces apoptosis of a neoplastic cell to which it binds, but does not induce apoptosis of a non-neoplastic cell.
- 30 7. The purified polypeptide of claim 1, 2 or 3 wherein said polypep-

tide comprises an antibody or a functional fragment thereof.

- 5           8. The purified polypeptide of claim 7, wherein said polypeptide is a functional fragment selected from the group consisting of  $V_L$ ,  $V_H$ ,  $F_V$ ,  $F_C$ , Fab, Fab', and  $F(ab')_2$ .
- 10          9. The purified polypeptide of claim 8, wherein said polypeptide has an amino acid sequence of the variable region of the light chain ( $V_L$ ) substantially identical to SEQ ID NO 1 or/and an amino acid sequence of the variable region of the heavy chain ( $V_H$ ) substantially identical to SEQ ID NO 3.
- 15          10. The purified polypeptide of claim 8, wherein said polypeptide has a nucleic acid sequence of the variable region of the light chain ( $V_L$ ) substantially identical to SEQ ID NO 2 or/and a nucleic amino acid sequence of the variable region of the heavy chain ( $V_H$ ) substantially identical to SEQ ID NO 4.
- 20          11. The purified polypeptide of claim 8, wherein said functional fragment comprises a fragment of the sequence of SEQ ID NO:1 and SEQ ID NO:3.
- 25          12. The purified polypeptide of claim 8, wherein said functional fragment comprises a fragment that is substantially identical to the sequence of SEQ ID NO:1 or SEQ ID NO:3.
- 30          13. The purified polypeptide of claim 1, 2, or 3, wherein said polypeptide comprises a sequence that is substantially identical to the amino acid sequence of SEQ ID NO:1.

14. The purified polypeptide of claim 1, 2 or 3, wherein said polypeptide comprises a sequence that is substantially identical to the amino acid sequence of SEQ ID NO:3.
- 5 15. The purified polypeptide of claim 1, 2 or 3, wherein said polypeptide comprises a nucleic acid sequences that are substantially identical to nucleotides 67-99 (CDR1), 145-165 (CDR2) and 262-288 (CDR3) of SEQ ID NO 2.
- 10 16. The purified polypeptide of claim 1, 2, or 3, wherein said polypeptide comprises a nucleic acid sequences that are substantially identical to nucleotides 91-105 (CDR1), 148-198 (CDR2) and 295-330 (CDR3) of SEQ ID NO 4.
- 15 17. A purified polypeptide comprising the amino acid sequence of SEQ ID NO:1.
18. A purified polypeptide comprising the amino acid sequence of SEQ ID NO:3.
- 20 19. A purified polypeptide comprising the amino acid sequence of SEQ ID NO:1 and/or SEQ ID NO: 3.
- 25 20. A purified polypeptide of claim 1, 2, 3, 4, 5, 6, 17, 18 or 19 having at least one complementarity-determining regions (CDR) or functional fragments thereof comprising the amino acid sequence substantially identical to the amino acid sequence Ser-Gly-Asp-Lys-Leu-Gly-Asp-Lys-Tyr-Ala-Cys (CDR1) or Gln-Asp-Ser-Lys-Arg-Pro-Ser (CDR2) or Gln-Ala-Trp-Asp-Ser-Ser-Ile-Val-Val (CDR3) of SEQ ID NO: 1 and/or Ser-Tyr-Ala-Met-His (CDR1) or
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Val-Ile-Ser-Tyr-Asp-Gly-Ser-Asn-Lys-Tyr-Tyr-Ala-Asp-Ser-Val-  
Lys-Gly (CDR2) or Asp-Arg-Leu-Ala-Val-Ala-Gly-Lys-Thr-Phe-  
Asp-Tyr (CDR3) SEQ ID NO: 3.

- 5           21. The purified polypeptide of claim 1, 2, 3, 4, 5, 6, 17, 18, 19 or 20,  
            wherein said polypeptide is a monoclonal antibody.
22. The purified polypeptide of claim 21, wherein said monoclonal  
            antibody is a human monoclonal antibody.
- 10           23. A cell that expresses the polypeptide of claim 1, 2 or 3.
24. A cell that expresses a polypeptide that comprises a sequence  
            that is substantially identical to the amino acid sequence of SEQ  
15           ID NO:1.
25. The cell of claim 24, wherein said polypeptide comprises the se-  
            quence of SEQ ID NO:1.
- 20           26. A cell that expresses a polypeptide that comprises a sequence  
            that is substantially identical to the amino acid sequence of SEQ  
            ID NO:3.
27. The cell of claim 26, wherein said polypeptide comprises the se-  
25           quence of SEQ ID NO:3.
28. A cell that expresses a polypeptide that comprises the amino acid  
            sequence of SEQ ID NOS:1 and 3.

29. The cell of any one of claims 23-28, wherein said cell is a hybridoma.

30. A method of generating the cell of claim 29, said method comprising the steps of:

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(a) contacting lymphocytes with a heteromyeloma cell line under conditions that result in the fusion of a lymphocyte with a heteromyeloma cell, said fusion resulting in a hybridoma,

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(b) determining whether said hybridoma produces a polypeptide that inhibits proliferation in a neoplastic cell to which it binds, but does not inhibit proliferation in a non-neoplastic cell and

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(c) determining whether said hybridoma produces a polypeptide that specifically binds to BXPC-3 (ATCC Accession No. CRL-1687), 23132/87 (DSMZ Accession No. ACC 201), COLO-206F (DSMZ Accession No. ACC 21), COLO-699 (DSMZ Accession No. ACC 196), and LOU-NH91 (DSMZ Accession No. ACC 393) cells and not to non-neoplastic cells.

31. A method of generating the cell of claim 29, said method comprising the steps of:

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(a) contacting lymphocytes with a heteromyeloma cell line under conditions that result in the fusion of a lymphocyte with a heteromyeloma cell, said fusion resulting in a hybridoma,

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(b) determining whether said hybridoma produces a polypeptide that induces intracellular accumulation of lipids in a neoplastic cell to which it binds, but does not induce intracellular accumulation of lipids in a non-neoplastic cell and

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(c) determining whether said hybridoma produces a polypeptide that specifically binds to BXPC-3 (ATCC Accession No. CRL-1687), 23132/87 (DSMZ Accession No. ACC 201), COLO-206F

to which it binds, but does not induce intracellular accumulation of lipids in a non-neoplastic cell and

(c) determining whether said hybridoma produces a polypeptide that specifically binds to BXPC-3 (ATCC Accession No. CRL-1687), 23132/87 (DSMZ Accession No. ACC 201), COLO-206F (DSMZ Accession No. ACC 21), COLO-699 (DSMZ Accession No. ACC 196), and LOU-NH91 (DSMZ Accession No. ACC 393) cells and not to non-neoplastic cells.

32. A method of generating the cell of claim 29, said method comprising the steps of:

(a) contacting lymphocytes with a heteromyeloma cell line under conditions that result in the fusion of a lymphocyte with a heteromyeloma cell, said fusion resulting in a hybridoma,

(b) determining whether said hybridoma produces a polypeptide that induces apoptosis of a neoplastic cell to which it binds, but does not induce apoptosis of a non-neoplastic cell, and

(c) determining whether said hybridoma produces a polypeptide that specifically binds to BXPC-3 (ATCC Accession No. CRL-1687), 23132/87 (DSMZ Accession No. ACC 201), COLO-206F (DSMZ Accession No. ACC 21), COLO-699 (DSMZ Accession No. ACC 196), and LOU-NH91 (DSMZ Accession No. ACC 393) cells and not to non-neoplastic cells.

33. Use of the purified polypeptide of claim 1, 2, 3, 4, 5, 6, 17, 18, 19 or 20 in a method of diagnosing a neoplasm in a mammal, said method comprising the steps of:

(a) contacting a cell or tissue sample of said mammal with the purified polypeptide of claim 1, 2, 3, 4, 5, 6, 17, 18, 19 or 20 and



(b) detecting whether said purified polypeptide binds to said cell or tissue sample, wherein binding of said purified polypeptide to said cell or tissue sample is indicative of said mammal having a neoplasm.

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34. The use of claim 33, wherein said mammal is a human.

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35. The use of claim 33, wherein said neoplasm is a adenocarcinoma of the lung, squamous cell lung carcinoma, intestinal type gastric carcinoma, diffuse type gastric carcinoma, adenocarcinoma of the colon, adenocarcinoma of the prostate, squamous cell carcinoma of the esophagus, adenocarcinoma of the esophagus, lobular carcinoma of the breast, ductal carcinoma of the breast, adenocarcinoma of the pancreas, adenocarcinoma of the ovary, and

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adenocarcinoma of the uterus cell.

36. The use of claim 33, wherein said polypeptide is an antibody.

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37. The use of claim 33, wherein said polypeptide is conjugated to a detectable agent selected from the group consisting of a radionuclide, a fluorescent marker, an enzyme, a cytotoxin, a cytokine, and a growth inhibitor.

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38. The use of claim 33, wherein said polypeptide is conjugated to a protein purification tag.

39. The use of claim 38, wherein said protein purification tag is cleavable.

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40. Use of the purified polypeptide of claim 1, 2, 3, 4, 5, 6, 17, 18, 19



5 or 20 in a method of treating a proliferative disorder in a mammal, said method comprising the step of contacting a cell or tissue sample with the purified polypeptide of claim 1, 2, 3, 4, 5, 6, 18, 19, 20 or 21, wherein binding of said purified polypeptide to said cell or tissue sample results in a reduction in proliferation of said cell or of a cell in said tissue sample.

41. The use of claim 40, wherein said mammal is a human.

10 42. The use of claim 40, wherein said proliferative disorder is a adenocarcinoma of the lung, squamous cell lung carcinoma, intestinal type gastric carcinoma, diffuse type gastric carcinoma, adenocarcinoma of the colon, adenocarcinoma of the prostate, squamous cell carcinoma of the esophagus, adenocarcinoma of the esophagus, lobular carcinoma of the breast, ductal carcinoma of the breast, adenocarcinoma of the pancreas, adenocarcinoma of the ovary, and adenocarcinoma of the uterus.

20 43. The use of claim 40, wherein said polypeptide is an antibody.

25 44. The use of claim 40, wherein said polypeptide is conjugated to a detectable agent selected from the group consisting of a radionuclide, a fluorescent marker, an enzyme, a cytotoxin, a cytokine, and a growth inhibitor.

45. The use of claim 44, wherein said detectable agent is capable of inhibiting cell proliferation of said cell or tissue sample.

30 46. The use of claim 44, wherein said polypeptide is conjugated to a protein purification tag.

47. The use of claim 46, wherein said protein purification tag is cleavable.

5 48. Use of the purified polypeptide of claim 1, 2, 3, 4, 5, 6, 17, 18, 19  
or 20 in a method of treating a proliferative disorder in a mammal,  
said method comprising the step of contacting a cell or tissue  
sample with the purified polypeptide of claim 1, 2, 3, 4, 5, 6, 18,  
19, 20 or 21, wherein binding of said purified polypeptide to said  
10 cell or tissue sample results in the intracellular accumulation of  
lipids of said cell or of a cell in said tissue sample.

49. The use of claim 48, wherein said mammal is a human.

15 50. The use of claim 48, wherein said proliferative disorder is a ade-  
nocarcinoma of the lung, squamous cell lung carcinoma, intestinal  
type gastric carcinoma, diffuse type gastric carcinoma, adenocar-  
cinoma of the colon, adenocarcinoma of the prostate, squamous  
cell carcinoma of the esophagus, adenocarcinoma of the esopha-  
gus, lobular carcinoma of the breast, ductal carcinoma of the  
20 breast, adenocarcinoma of the pancreas, adenocarcinoma of the  
ovary, and adenocarcinoma of the uterus.

51. The use of claim 48, wherein said polypeptide is an antibody.

25 52. The use of claim 48, wherein said polypeptide is conjugated to a  
detectable agent selected from the group consisting of a radionu-  
clide, a fluorescent marker, an enzyme, a cytotoxin, a cytokine,  
and a growth inhibitor.

53. The use of claim 52, wherein said detectable agent is capable of inhibiting cell proliferation of said cell or tissue sample.

5 54. The use of claim 52, wherein said polypeptide is conjugated to a protein purification tag.

55. The use of claim 54, wherein said protein purification tag is cleavable.

10 56. Use of the purified polypeptide of claim 1, 2, 3, 4, 5, 6, 17, 18, 19 or 20 in a method of treating a proliferative disorder in a mammal, said method comprising the step of contacting a cell or tissue sample with the purified polypeptide of claim 1, 2, 3, 4, 5, 6, 17, 18, 19 or 20 wherein binding of said purified polypeptide to said  
15 cell or tissue sample results in the induction of apoptosis of said cell or tissue sample.

57. The use of claim 56, wherein said mammal is a human.

20 58. The use of claim 56, wherein said proliferative disorder is a adenocarcinoma of the lung, squamous cell lung carcinoma, intestinal type gastric carcinoma, diffuse type gastric carcinoma, adenocarcinoma of the colon, adenocarcinoma of the prostate, squamous cell carcinoma of the esophagus, adenocarcinoma of the esophagus,  
25 lobular carcinoma of the breast, ductal carcinoma of the breast, adenocarcinoma of the pancreas, adenocarcinoma of the ovary and adenocarcinoma of the uterus

59. The use of claim 56, wherein said polypeptide is an antibody.

5 60. The use of claim 56, wherein said polypeptide is conjugated to a detectable agent selected from the group consisting of a radionuclide, a fluorescent marker, an enzyme, a cytotoxin, a cytokine, and a growth inhibitor.

10 61. The use of claim 60, wherein said detectable agent is capable of inducing apoptosis of said cell or tissue sample.

62. The use of claim 60, wherein said polypeptide is conjugated to a protein purification tag.

15 63. The use of claim 62, wherein said protein purification tag is cleavable.

20 64. Purified polypeptide of any one of claims 1, 2, 3, 4, 5, 6, 17, 18, 19 or 20 in a pharmaceutically acceptable carrier for the production of a medicament that inhibits cell proliferation.

25 65. Purified polypeptide of any one of claims 1, 2, 3, 4, 5, 6, 17, 18, 19 or 20 in a pharmaceutically acceptable carrier for the production of a medicament that induces the intracellular accumulation of lipids.

66. Purified polypeptide of any one of claims 1, 2, 3, 4, 5, 6, 17, 18, 19 or 20 in a pharmaceutically acceptable carrier for the production of a medicament that induces apoptosis.

67. Purified polypeptide of any one of claims 1, 2, 3, 4, 5, 6, 17, 18, 19 or 20 in a pharmaceutically acceptable carrier for the production of a medicament that inhibits cell proliferation and induces the intracellular accumulation of lipids and induces apoptosis.

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68. A diagnostic agent comprising the purified polypeptide of any one of claims 1, 2, 3, 4, 5, 6, 17, 18, 19 or 20.

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69. An isolated nucleic acid molecule comprising the sequence of SEQ ID NO:2 or 4.

70. A vector comprising the nucleic acid molecule of claim 69.

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71. A cell comprising the vector of claim 70.